71. The method of claim 63, wherein the locus ceruleus is damaged due to Parkinson's disease.--

REMARKS

I. Amendment

Support for the revisions to the claims is found on page 9 of the specification. Support for the new claims may be found on pages 5, 17, 18, and 19 of the specification.

II. Status of the claims

Claims 40, 43, 46, and 57 are amended, and new claims 68-71 are added.

Upon entry of the above amendment, claims 24-71 are pending.

The attached Appendix recites those pending claims.

III. Rejection under 35 U.S.C. § 102

Claims 24-67 are rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Lewis et al. (A1). The Examiner alleges that Lewis et al. teach a method for "treatment for diseases such as Alzheimer's disease, stroke, epilepsy, amyotrophic lateral sclerosis, or Parkinson's disease by administering an effective amount of IGF I or IGF II or a combination thereof." Examiner further alleges that "the treatment by the parenteral administration of IGF I or IGF II to treat these diseases comprise a nonintracranial administration of an IGF in an amount to [sic] effective to treat the locus ceruleus neurons". Applicant respectfully traverses this rejection.

Upon entry of the above amendment, all pending claims are directed to the parenteral nonintracranial administration of IGF. Applicant emphatically contends that Lewis et al. does not teach parenteral nonintracranial administration of unmodified IGF peptides. Applicant would like to draw Examiner's attention to the following passages:

> Where the polypeptide is intended for use as a therapeutic for disorders of the CNS, an additional problem must be addressed: overcoming the so-called "blood-

> brain barrier," the brain capillary wall structure that effectively screens out all but selected categories of molecules present in the blood, preventing their passage into the brain. While the blood-brain barrier may be effectively bypassed by direct infusion of the polypeptide into the brain, the search for a more practical method has focused on enhancing transport of the polypeptide of interest across the blood-brain barrier, such as by making the polypeptide more lipophilic, by conjugating the polypeptide of interest to a molecule which is naturally transported across the barrier, or by reducing the overall length of the polypeptide chain.

Lewis et al., col. 3, lines 44-58. Applicant specifically notes that the tone and emphasis of this passage teach that unmodified IGF molecules do not cross the blood-brain barrier.

Lewis et al. further brings this point home by repeatedly indicating that their method is directed toward modified or truncated forms of IGF. Lewis et al. teach that diseases such as Alzheimer's and Parkinson's are therapeutically "administering to the animal an effective amount of a functional derivative, e.g. a fragment or analog of IGF-I or of IGF-II" (column 4, lines 3-5; emphasis added). A method for enhancing the cholinergic activity of cholinergic neuronal cells is taught to be accomplished by "administering to the mammal an effective amount of a functional derivative of IGF-I or IGF-II, preferably a fragment of IGF-I, of IGF-II or, alternatively, an analog of IGF-I , of IGF-II, or of a fragment of IGF-I or IGF-II" (column 4, lines 16-20; emphasis added). Furthermore, Lewis et al recite that "[t]he method of the invention uses functional derivatives of IGF-I and of IGF-II to enhance the survival rate and/or the cholinergic activity of mammalian cells at an increased risk of death due to some factor such as disease, injury, or natural aging process" (column 4, lines 31-35; emphasis added). Finally, Lewis et al. specifically teach that their "invention is directed to the modification of neuroactive polypeptides such as IGF-I and IGF-II and their functional derivatives" (column 5, lines 60-62; emphasis added).

Applicant unequivocally disagrees with the Examiner's allegation that Lewis et al. teaches a method that "comprise[s] a *nonintracranial* administration" of IGF-I or IGF-II (emphasis added). Lewis et al. teaches the following in the examples: **1)** in vitro methods for measuring effectiveness of IGF treatment (Examples 1-3); **2)** intracerebral administration of IGF (Examples 4 and 5); **3)** methods for modifying IGF's (Examples 6-10); and **4)** a method for measuring the effectiveness of the IGF modifications (Example 11). Applicant contends that nowhere does Lewis et al. teach or even suggest the administration of IGF's via a parenteral nonintracranial method. On the contrary, Lewis et al. emphatically and unmistakably teach that IGF-I or IGF-II must either be modified or be delivered intracranially. Consequently, Applicant submits that rejection of claims 24-67 under 35 U.S.C. § 102(e) should be withdrawn.

Claims 40 and 42 are rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Gluckman et al. ((A62); BBRC, 1992). Applicant respectfully traverses this rejection.

Gluckman et al. recites administration of hIGF-I via "a single stereotaxic injection". It is further explained that this refers to an injection made "into the lateral ventricle of the injured hemisphere" (page 595, first full paragraph). It is clear from this passage that Gluckman et al. delivered the IGF intracranially. Upon entry of the above amendment claims 40 and 42 teach that the amount of circulating IGF is increased by administering IGF-I via a parenteral nonintracranial method. In view of the above Amendment and Remarks, the rejection of claims 40 and 42 under 35 U.S.C. § 102(a) as allegedly being anticipated by Gluckman et al. should be withdrawn.

Claims 40-42 are rejected under 35 U.S.C. § 102 (b) as being anticipated by Aroonsakul ((A51); U.S. Pat. No. 4,898,856). The Examiner alleges that these "claims encompass *indirect*

increase in bloodstream of IGF-I because of the limitation 'increasing the circulating concentration'" (emphasis). Applicant respectfully traverses this rejection.

Upon entry of the above amendment claims 40-42 are directed to an increased level of IGF-I resulting from parenteral nonintracranial administration of IGF-I. This amendment overcomes the Examiner's concern for claims that encompass an indirect increase in IGFs. Therefore, the rejection of claims 40–42 as allegedly being anticipated by Aroonsakul has been overcome and should be withdrawn.

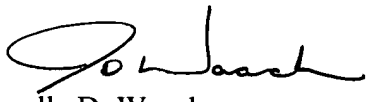
IV. Conclusion

In view of the above amendment and remarks Applicant believes that all rejections have been overcome and that the pending claims are in condition for allowance.

Should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Arnold White & Durkee Deposit Account No. 01-2508/CUSA019--1/WAA.

The Examiner is invited to contact the undersigned attorney at (713) 787-1686 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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